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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/016,869	01/30/1998	DAVID H. BEACH	GPCI-P10-071	7533

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ROPES & GRAY
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER
ROARK, JESSICA H

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/02/2002

39

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/016,869	BEACH ET AL.	
	Examiner	Art Unit	
	Jessica H. Roark	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *91-112* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *91-112* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 January 1998* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 9/9/02 (Paper No. 37), is acknowledged.
Claims 11, 58, 61-64, 66, 68-70, 72-76 and 83-90 have been cancelled.
Claims 1-10, 12-57, 59-60, 65, 67, 71 and 77-82 have been cancelled previously.
Claims 91-112 have been added.

Claims 91-112 are pending and are under consideration in the instant application.

Applicant's provision of a clean claim set is appreciated.

2. This Office Action will be in response to applicant's arguments, filed 9/9/02 (Paper No. 37). The rejections of record can be found in the previous Office Action (Paper No. 36).

It is noted that New Grounds of Rejection are set forth herein.

3. Applicant's cancellation of claims 11, 58, 61-64, 66, 68-70, 72-76 and 83-90 has obviated the previous objections and rejections with respect to these claims.

Any rejection of record in Paper No. 36 that applies to the newly added claims has been reiterated below, and Applicant's arguments, filed 9/9/02, addressed in the context of the application of the rejection of record to the newly added claims.

Drawings

4. Drawings have been submitted which fail to comply with 37 CFR 1.84.
Please see the enclosed form PTO-948.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. *The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.*

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

*Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.*

Related Applications Data

5. Applicant is requested to clarify the relationship of PCT/US93/09945 (filed 10/18/93) listed in the "Related Applications" section as amended 3/23/00. In particular, Applicant should identify the relationship (371, CON) of PCT/US93/09945 to its child and parent applications.

Specification

6. Applicant's amendment, filed 9/9/02, has obviated the previous objection to the Title and Specification.

7. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter in claims 91 and 103 of an "antibody preparation". See 37 CFR 1.75(d)(1) and MPEP 608.01(o).

While it is noted that "antibody preparation" was recited in original claim 11, the Examiner has been unable to clearly identify antecedent basis for this phrase in the specification. Applicant is requested to either point to support in the specification as filed, amend the specification to provide proper antecedent basis, or to amend the claims to recite an -- isolated antisera -- which is clearly supported in the specification as filed on page 33.

Claim Objections

8. Claim 111 is objected to for the following informalities: the claim recites in the second line "the anti-CR antibody" when it appears -- the anti-CCR antibody -- was intended.
Appropriate correction is required.

9. It is noted for examination purposes that the "antibody preparations" recited in claims 91 and 103 are considered to be isolated or otherwise purified antibodies that are part of a composition.

Claim Rejections - 35 USC § 112 second paragraph

10. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 95-97 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 95-97 recite the limitation "the anti-p16 antibody". However, there is insufficient antecedent basis for this limitation in these claims because claim 94, from which claims 95-97 depend, does not recite an anti-p16 antibody.

It is suggested that Applicant amend the claims to recite -- the antibody specifically immunoreactive with the 16 kD protein --.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

35 U.S.C. §§ 102 and 103

12. The rejections under 35 U.S.C. §§ 102 and 103 set forth below are made under the following assumptions regarding the effective filing date for the instantly claimed invention:

13. The Examiner acknowledges that pages 22-23 of USSN 07/991,997 (12/17/92) supports "antisera".

The Examiner also acknowledges that the support pointed to by Applicant in the Response filed 9/9/02 on page 22 of USSN 07/991,997 (12/17/92) does appear to provide an adequate written support of antibodies specifically reactive with the p16 component of the p16-CDK4 complex.

It is again acknowledged that both USSN 08/154,915 (11/18/93) and USSN 07/991,997 appear to provide adequate written support for an antibody to a 16 kD protein that co-precipitates with CDK4 from lysates of SV40-transformed WI38 cells in the presence of an anti-CDK4 antibody.

It is also again acknowledged that antibodies to a polypeptide comprising SEQ ID NO:35 appear to have adequate written support in USSN 08/154,915 (11/18/93) and PCT/US93/09945 (10/18/93).

However, the Examiner was still unable to identify written support for antibody fragments, including Fab and F(ab')2 fragments, in either the '915 or '997 applications.

Thus the priority date of instant claims 92-102 and 104-112, reciting fragments, appears to be at least *5/25/94, but not 11/18/93.*

In addition, it appears that the priority documents '915 and '997 do not provide adequate written support for an "antibody preparation", as recited in instant claims 91 and 103.

Thus the effective filing date of instant claims 91 and 103, reciting an "antibody preparation", also appears to be at least *5/25/94, but not 11/18/93.*

It is noted that a particular form of antibody preparation, an isolated antisera, does appear to have adequate written support in the '915 and '997 priority documents.

Applicant is invited to point to clear support for the above noted limitations of antibody fragments and preparations.

Claim Rejections – 35 U.S.C. §§ 102 and 103

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

15. Claims 91-95, 98-99, 101-110 and 112 are rejected under 35 U.S.C. 102(e) as being anticipated by Kamb (US Pat No. 6,090,578, of record, see entire document).

Applicant's cancellation of claims 66 and 73 in the Amendment filed 9/9/02 has obviated the rejection of record in Paper No. 36. However, the instant claims for the reasons noted supra do not appear to be entitled to an effective filing date that pre-dates the earliest effective filing date of Kamb.

Kamb teaches and claims an antibody which binds a mammalian MTS1 polypeptide (see entire document, including claims). Kamb also teaches that the MTS1 polypeptide and p16 are the same protein (see entire document; e.g. column 16, especially lines 53-65; column 38, especially lines 51-67; and SEQ ID NO:2 of Kamb). Kamb teaches that the p16/MTS1 protein is a cell cycle regulatory protein that binds the cyclin-dependent kinase CDK4 (see columns 43-45, especially column 44 at lines 13-35). Kamb teaches that the anti-MTS1/p16 antibodies may be polyclonal, monoclonal, or antibody fragments (e.g., columns 14-15 and 55-56). Kamb also teaches that the purified antibodies may be labeled with a detectable label (e.g., column 15 at lines 24-40 and column 27-28). In addition, Kamb teaches diagnostic kits for detecting the MTS1/p16 cell cycle regulatory protein comprising antibodies to the p16/MTS1 cell cycle regulatory protein (e.g. columns 27-28 in view of columns 15 and 55-56).

Therefore the teachings of the reference anticipate the instant invention.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of antibodies to a p16/MST1 protein. It is noted that p16/MST1 is inherently a 16 kD protein that coprecipitates with CDK4 from lysate of SV40-transformed WI38 cells in the presence of an anti-CDK4 antibody, and is inherently a protein comprising SEQ ID NO:35.

16. Claims 91-95, 98-99, 101-110 and 112 are rejected under 35 U.S.C. 102(e) as being anticipated by Skolnick et al. (US Pat No. 5,624,819, of record; see entire document).

Applicant's cancellation of claims 66 and 73 in the Amendment filed 9/9/02 has obviated the rejection of record in Paper No. 36. However, the instant claims for the reasons noted supra do not appear to be entitled to an effective filing date that pre-dates the earliest effective filing date of Skolnick et al.

Skolnick et al. teach an antibody which binds a mammalian MTS1 polypeptide (see entire document). Skolnick et al. also teach that the MTS1 polypeptide and p16 are the same protein (see entire document; e.g. column 16, especially lines 43-54; column 38, especially lines 1-16; and SEQ ID NO:2). Skolnick et al. teach that the p16/MTS1 protein is a cell cycle regulatory protein that binds the cyclin-dependent kinase CDK4 (see columns 43-44, especially column 43 at lines 9-50). Skolnick et al. teach that the anti-MTS1/p16 antibodies may be polyclonal, monoclonal, or antibody fragments (e.g., columns 14-15 and 54-55); and that the purified antibodies may be labeled with a detectable label (e.g., column 15 at lines 20-31 and column 27). In addition, Skolnick et al. teach diagnostic kits for detecting the MTS1/p16 cell cycle regulatory protein comprising antibodies to the p16/MTS1 cell cycle regulatory protein (e.g., column 27 in view of columns 15 and 54-55).

Therefore the teachings of the reference anticipate the instant invention.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of antibodies to a p16/MST1 protein. It is noted that p16/MST1 is inherently a 16 kD protein that coprecipitates with CDK4 from lysate of SV40-transformed WI38 cells in the presence of an anti-CDK4 antibody, and is inherently a protein comprising SEQ ID NO:35.

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 91-112 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xiong et al. (Genes & Dev. August 1993; 7:1572-1583, IDS #EO) in view of Busch et al. (US Pat No. 4,794,077, of record).

Applicant's arguments, filed 9/9/02, have been fully considered but have not been found convincing.

Applicant argues that in view of the amendment filed 9/9/02 and the support provided in the '997 application, the Xiong et al. reference is antedated.

However, although certain limitations are support in the '997 application as acknowledged supra; the instant claims still contain limitations which do not appear to have adequate written support in the '997 application.

Consequently, the Xiong et al. reference published in August 1993 is available as prior art under 35 USC 102(a) with respect to all pending claims.

In addition, Applicant has provided a Declaration under 37 CFR 1.132 by Inventor Beach.

However, the Beach Declaration under 37 CFR 1.132 filed 9/9/02 is insufficient to overcome the rejection of claims 91-112 based upon Xiong et al. publication because Demetrick, Serrano and Hannon are not co-authors on the Xiong et al. publication. Thus the printed publication is still by "another" and available as prior art under 35 USC 102(a).

Although a reference that is not a statutory bar under 35 USC 102(b) may be antedated, in order to antedate a reference a proper Declaration under 37 CFR 1.131 (or 37 CFR 1.132, if appropriate) must be filed (MPEP 7.15.01(d).

Therefore, Xiong et al. is still available as a reference under 35 USC 102(a) with respect to the instant claims.

The rejection of record in Paper No. 36 is reiterated below as applied to the instantly pending claims:

The claims are drawn to antibodies, antibody preparations and kits comprising antibodies to a 16 kD protein that coprecipitates with CDK4 from lysate of SV40-transformed WI38 cells in the presence of an anti-CDK4 antibody (which is the same as a protein comprising SEQ ID NO:35).

Xiong et al. teach a p16 cell cycle regulatory protein that is 16 kD and that binds to and coprecipitates with the cyclin-dependent kinase CDK4 from cell lysate of SV40-transformed WI38 cells in the presence of an anti-CDK4 antibody (see entire document, especially Figure 1). Xiong et al. teach that the molecular identity of p16 was unknown, but that it associates with proteins involved in cell cycle progression that are altered in oncogenically transformed cells, and that studies addressing possible altered responses involving cell cycle regulatory proteins are important to understanding oncogenesis (e.g., see "Discussion"). Xiong et al. purify p16 from several human cellular sources, including the WI38 cell line transformed with SV40 (the VA13 cell line, see "Cell Culture" on page 1581) and provide a peptide map to show that p16 is the same in each case (e.g., Figure 6). Xiong et al. also teach the production of antibodies to other proteins involved in cell cycle regulation (see entire document, especially "Antibodies and Immunological Methods" on page 1581), and use these antibodies to study the association and expression of various cell cycle proteins (see entire document).

Xiong et al. do not teach an antibody, antibody preparation, or kit comprising an antibody to a 16 kD protein that coprecipitates with CDK4 from lysate of SV40-transformed WI38 cells in the presence of an anti-CDK4 antibody, nor an antibody to p16.

Busch et al. teach and claim a kit comprising an antibody to a cell cycle regulatory protein (p145) and a detectable label for detecting the antibody (see entire document, especially claims 3-15 and column 11). Means for detecting the cell cycle regulatory protein are taught that include both a detectable label conjugated to the antibody (e.g. column 11 at lines 15-26 and claim 16) and a second antibody (e.g., column 11 at lines 27-41). Both monoclonal and purified polyclonal antibody preparations are taught (see entire document, especially claims 3-5 and 14-15). Busch et al. teach throughout the reference that the antibodies are formulated for detecting the protein in samples of cells (e.g., columns 7-8).

Given the teachings of the references, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare antibodies, antibody preparations, and kits comprising antibodies to the p16 taught by Xiong et al. Given the teachings of Xiong et al. that p16 is associated with CDK4 and involved in cell cycle progression and possibly the mechanism underlying oncogenesis, one of ordinary skill in the art would have been motivated to provide an antibody, antibody preparation, or kit comprising an antibody to p16 in order to study p16's role in cell cycle and oncogenesis. As taught by both Xiong et al. and Busch et al., one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of successfully producing antibodies to p16 and formulating them in various diagnostic kits for detecting p16 in a sample of cells. Although the amino acid sequence of p16 is not taught by either reference, the sequence in an intrinsic property of the protein and thus a recitation of sequence composition does not render an antibody to the protein unobvious. Finally, although Fab and $F(ab')_2$ fragments are not taught explicitly by either reference, these forms of antibodies were well known to one of ordinary skill in the art at the time the invention was made. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

19. Claims 96-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Kamb (US Pat No. 6,090,578, of record), or Skolnick et al. (US Pat No. 5,624,819, of record) in view of Owens et al. (J. Immunol. Methods February 1994; 168:149-165, of record).

Applicant's cancellation of claims 62-63 and 74-75 in the Amendment filed 9/9/02 has obviated the rejection of record in Paper No. 36. However, the instant claims for the reasons noted supra do not appear to be entitled to an effective filing date that pre-dates the earliest effective filing date of Kamb or Skolnick et al. Therefore, the rejection of record in Paper No. 36 is applicable to the instant claims

The claims are drawn to Fab and $F(ab')_2$ fragments of an antibody to a 16 kD protein that coprecipitates with CDK4 from lysate of SV40-transformed WI38 cells in the presence of an anti-CDK4 antibody.

Both Kamb and Skolnick et al. have been discussed supra.

Although both Kamb and Skolnick et al. teach antibody fragments specifically reactive with a 16 kD protein that coprecipitates with CDK4 from lysate of SV40-transformed WI38 cells in the presence of an anti-CDK4 antibody; neither Kamb nor Skolnick et al. exemplify Fab and $F(ab')_2$ fragments.

Owens et al. teach that it was well known in the art that antibody fragments were the reagent of choice for some clinical applications (see entire document, but especially comment on page 149, 2nd paragraph). Owens et al. also teach that Fab and $F(ab')_2$ fragments are the fragments typically produced, and have been invaluable as diagnostic reagents (e.g., page 155, 2nd column).

In view of the art-recognized applicability of Fab and $F(ab')_2$ fragments for a variety of diagnostic applications, as taught by Owens et al.; it would have been obvious to the ordinary artisan at the time the invention was made to formulate the antibody fragments taught by either Kamb or Skolnick et al. as Fab and $F(ab')_2$ fragments. The ordinary artisan would have been motivated to select Fab and $F(ab')_2$ fragments in view of the established utility of Fab and $F(ab')_2$ fragments in diagnostic applications, as taught by Owens et al. Given that the techniques for producing Fab and $F(ab')_2$ fragments were well established at the time the invention was made, the ordinary artisan would have had a reasonable expectation of successfully producing Fab and $F(ab')_2$ fragments. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

20. No claim is allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica H. Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday, 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
November 27, 2002

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
12/4/02